Pharmacogenomic Testing for Drug Toxicity and Response

For the purposes of this guideline, pharmacogenomic tests are those performed to predict or assess an individual’s response to therapy as well as the risk of toxicity from drug treatment. Testing may be performed prior to treatment in order to determine if the individual has genetic mutations that could affect drug response and/or increase the risk for adverse drug reactions. Testing may also be performed during treatment to assess whether an individual is having an adequate response or investigate the cause of an unexpected or adverse reaction.

Companion diagnostics are assays that help determine whether a drug may be safe or effective for a particular patient. Companion assays are evaluated as part of the Food & Drug Administration’s (FDA’s) development and approval process for the new drug. According to the FDA, “A companion diagnostic is a medical device, often an in vitro device, which provides information that is essential for the safe and effective use of a corresponding drug or biological product. The test helps a health care professional determine whether a particular therapeutic product’s benefits to patients will outweigh any potential serious side effects or risks.” ¹ Although specific companion diagnostic tests may be identified in the FDA label for a new drug approval, similar laboratory-developed tests (LDTs) performed by a CLIA-certified laboratory are generally accepted as alternatives that can typically provide the required information.

Complementary diagnostics are assays that were developed and in use prior to the FDA’s approval of a new drug. They are not evaluated through the FDA’s development and approval process for new drugs. Complementary diagnostics are used to help provide additional information about how a drug might be used, or whether someone should receive a certain class of drugs. These tests are not specifically required for the safe and effective use of a drug, which is part of what differentiates them from companion diagnostics. As with companion diagnostics, LDTs that are similar to the defined complementary diagnostic, when performed by a CLIA-certified laboratory, are able to provide the same information.²

Criteria

Criteria: General Coverage Guidance

Pharmacogenomic tests may be indicated when ALL of the following conditions are met:

• The individual is currently taking or considering treatment with a drug potentially affected by a known mutation that can be detected by a corresponding test.

• Technical and clinical validity: The test must be accurate, sensitive, and specific, based on sufficient, quality scientific evidence to support the claims of the test.
• Clinical utility: Healthcare providers can use the test results to guide changes in drug therapy management that will improve patient outcomes.
• Reasonable use: The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social, or ethical challenges.

Criteria: Companion Diagnostic Testing

Single gene testing for purposes of medication usage will be approved when the following criteria are met:
• Testing is being performed in a CLIA-certified laboratory, AND
• Testing of the requested gene has not previously been performed, AND
• A medication’s FDA label requires results from the genetic test to effectively or safely use the therapy in question, AND
• Healthcare providers can use the test results to directly impact medical care for the individual, OR
• The member meets all criteria in a test-specific guideline, if available

Criteria: Limits

Testing will be covered only for the number of genes or tests necessary to establish drug response. When available and cost-efficient, a tiered approach to testing, with reflex to more detailed testing and/or different genes, is recommended.

For pharmacogenomic tests that look for changes in germline DNA (i.e., not tumor DNA or viral DNA), testing will be allowed once per lifetime per gene. Exceptions may be considered if technical advances in testing or the discovery of novel genetic variants demonstrate significant advantages that would support a medical need to retest.

Testing performed in a CLIA-certified laboratory will be considered for coverage. The use of a specific FDA approved companion diagnostic is not necessary for coverage to be considered.

Criteria: Exclusions

Some pharmacogenomic tests are considered investigational and experimental, as they are not supported by existing evidence, professional guidelines and/or the FDA, or their use in medical management is deemed to be still evolving.

The following pharmacogenomic tests are considered investigational and experimental. This list is not intended to be all inclusive.
• 5HT2C (Serotonin Receptor) gene variants
• Ankyrin G gene variants
• COMT (Catechol Methyl Transferase) gene variants
• Catechol-O-Methyltransferase (COMT) Genotype from Mayo Clinic (CPT 0032U)
• CYP450 gene variants (including, but not limited to CYP1A2, CYP2D6, CYP2C9, CYP2C19, CYP3A4 [CPT 81230], CYP3A5 [CPT 81231]) for psychotherapeutic, cardiovascular, or general drug response
• Cytochrome P450 1A2 Genotype from Mayo Clinic (CPT 0031U)
• CYP2C19 testing for the management of H. pylori
• DRD2 (Dopamine Receptor) gene variants
• Focused Pharmacogenomics Panel from Mayo Clinic (CPT 0029U)
• IFNL3 rs12979860 gene variant (CPT 81283)
• KIF6 gene variants
• KRAS testing for response to erlotinib in non-small cell lung cancer
• MTHFR gene variants
• NAT2 gene variants
• OPRM1 gene variants
• Serotonin Receptor Genotype (HTR2A and HTR2C) from Mayo Clinic (CPT 0033U)
• SLC6A4 (5-HTTLPR) serotonin transporter variants
• Thiopurine Methyltransferase (TPMT) and Nudix Hydrolase (NUDT15) Genotyping from Mayo Clinic (CPT 0034U)
• Warfarin Response Genotype from Mayo Clinic (CPT 0030U)

Criteria: Test-specific Guidelines

Test-specific guidelines are available for some pharmacogenomic tests. Please see the guidelines manual for a list of test-specific guidelines. For tests without a specific guideline, use the General Coverage Guidance provided.

References

1. Companion diagnostics. U.S. Food & Drug Administration website. Available at: https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407297.htm


